**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

Cetrotide 0.25 mg powder and solvent for solution for injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 0.25 mg cetrorelix (as acetate).
After reconstitution with the solvent provided, each ml of the solution contains 0.25 mg cetrorelix.

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

Appearance of the powder: white lyophilisate
Appearance of the solvent: clear and colourless solution

The pH of the reconstituted solution is 4.0 – 6.0

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Prevention of premature ovulation in patients undergoing a controlled ovarian stimulation, followed by oocyte pick-up and assisted reproductive techniques.

In clinical trials Cetrotide was used with human menopausal gonadotropin (HMG), however, limited experience with recombinant follicule-stimulating hormone (FSH) suggested similar efficacy.

### 4.2 Posology and method of administration

Cetrotide should only be prescribed by a specialist experienced in this field.

The first administration of Cetrotide should be performed under the supervision of a physician and under conditions where treatment of possible allergic/pseudo-allergic reactions (including life-threatening anaphylaxis) is immediately available. The following injections may be self-administered as long as the patient is made aware of the signs and symptoms that may indicate hypersensitivity, the consequences of such a reaction and the need for immediate medical intervention.

The contents of 1 vial (0.25 mg cetrorelix) are to be administered once daily, at 24 h intervals, either in the morning or in the evening. Following the first administration, it is advised that the patient be kept under medical supervision for 30 minutes to ensure there is no allergic/pseudo-allergic reaction to the injection.

Cetrotide is for subcutaneous injection into the lower abdominal wall.

The injection site reactions may be minimised by rotating the injection sites, delaying injection at the same site and injecting the product in a slow rate to facilitate the progressive absorption of the product.

Administration in the morning: Treatment with Cetrotide should commence on day 5 or 6 of ovarian stimulation (approximately 96 to 120 hours after start of ovarian stimulation) with urinary or recombinant gonadotropins and is to be continued throughout the gonadotropin treatment period including the day of ovulation induction.

Administration in the evening: Treatment with Cetrotide should commence on day 5 of ovarian stimulation (approximately 96 to 108 hours after start of ovarian stimulation) with urinary or recombinant gonadotropins and is to be continued throughout the gonadotropin treatment period until the evening prior to the day of ovulation induction.

Additional information on special populations:

There is no relevant indication for the use of Cetrotide in children or geriatric populations.

For instructions for preparation, see section 6.6.

## 4.3 Contraindications

- Hypersensitivity to the active substance or any structural analogues of gonadotropin-releasing hormone (GnRH), extrinsic peptide hormones or to any of the excipients.
- Pregnancy and lactation.
- Postmenopausal women.
- Patients with moderate and severe renal and hepatic impairment.

## 4.4 Special warnings and precautions for use

Special care should be taken in women with signs and symptoms of active allergic conditions or known history of allergic predisposition. Treatment with Cetrotide is not advised in women with severe allergic conditions.

During or following ovarian stimulation an ovarian hyperstimulation syndrome can occur. This event must be considered as an intrinsic risk of the stimulation procedure with gonadotropins.

An ovarian hyperstimulation syndrome should be treated symptomatically, e.g. with rest, intravenous electrolytes/colloids and heparin therapy.

Luteal phase support should be given according to the reproductive medical centre´s practice.

There is limited experience up to now with the administration of Cetrotide during a repeated ovarian stimulation procedure. Therefore Cetrotide should be used in repeated cycles only after a careful risk/benefit evaluation.

## 4.5 Interaction with other medicinal products and other forms of interaction

*In vitro* investigations have shown that interactions are unlikely with medicinal products that are metabolised by cytochrome P450 or glucuronised or conjugated in some other way. However, although there has been no evidence of drug-interactions, especially with commonly used medicinal products, gonadotropins or products that may induce histamine release in susceptible individuals, the possibility of an interaction cannot be totally excluded.

## 4.6 Pregnancy and lactation

Cetrotide is not intended to be used during pregnancy and lactation (see section 4.3).

Studies in animals have indicated that cetrorelix exerts a dose related influence on fertility, reproductive performance and pregnancy. No teratogenic effects occurred when the medicinal product was administered during the sensitive phase of gestation.

## 4.7 Effects on ability to drive and use machines

Cetrotide has no or negligible influence on the ability to drive or use machines.

## 4.8 Undesirable effects

The most commonly reported side effects are local injection site reactions such as erythema, swelling and pruritus that are usually transient in nature and mild in intensity. In clinical trials, these effects were observed with a frequency of 9.4% following multiple injections of Cetrotide 0.25 mg.

Mild to moderate ovarian hyperstimulation syndrome (OHSS) (WHO grade I or II) have been commonly reported and should be considered as an intrinsic risk of the stimulation procedure. Inversely, severe OHSS remains uncommon.

Uncommonly, cases of hypersensitivity reactions including pseudo-allergic/anaphylactoid reactions have been reported.

The adverse reactions reported below are classified according to frequency of occurrence as follows:

| | |
|---|---|
| Very Common | ≥ 1/10 |
| Common | ≥ 1/100 to < 1/10 |
| Uncommon | ≥ 1/1,000 to < 1/100 |
| Rare | ≥ 1/10,000 to < 1/1,000 |
| Very rare | < 1/10,000 |

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

| | | |
|---|---|---|
| Immune system disorders | Uncommon | Systemic allergic/pseudo-allergic reactions including life-threatening anaphylaxis. |
| Nervous system disorders | Uncommon | Headache |
| Gastrointestinal disorders | Uncommon | Nausea |
| Reproductive system and breast disorders | Common | Mild to moderate ovarian hyperstimulation syndrome (WHO grade I or II) can occur which is an intrinsic risk of the stimulation procedure (see section 4.4). |
| | Uncommon | Severe ovarian hyperstimulation syndrome (WHO grade III) |
| General disorders and administration site conditions | Common | Local reactions at the injection site (e.g. erythema, swelling and pruritus) have been reported. Usually they were transient in nature and of mild intensity. The frequency as reported in clinical trials was 9.4% following multiple injections of 0.25 mg cetrorelix. |

## 4.9 Overdose

Overdosage in humans may result in a prolonged duration of action but is unlikely to be associated with acute toxic effects.

In acute toxicity studies in rodents non-specific toxic symptoms were observed after intraperitoneal administration of cetrorelix doses more than 200 times higher than the pharmacologically effective dose after subcutaneous administration.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-gonadotropin-releasing hormones, ATC code: H01CC02.

Cetrorelix is a luteinising hormone releasing hormone (LHRH) antagonist. LHRH binds to membrane receptors on pituitary cells. Cetrorelix competes with the binding of endogenous LHRH to these receptors. Due to this mode of action, cetrorelix controls the secretion of gonadotropins (LH and FSH).

Cetrorelix dose-dependently inhibits the secretion of LH and FSH from the pituitary gland. The onset of suppression is virtually immediate and is maintained by continuous treatment, without initial stimulatory effect.

In females, cetrorelix delays the LH surge and consequently ovulation. In women undergoing ovarian stimulation the duration of action of cetrorelix is dose dependent. Following a single dose of 3 mg of cetrorelix a duration of action of at least 4 days has been evaluated. On day 4 the suppression was approximately 70%. At a dose of 0.25 mg per injection repeated injections every 24 hours will maintain the effect of cetrorelix.

In animals as well as in humans, the antagonistic hormonal effects of cetrorelix were fully reversible after termination of treatment.

### 5.2 Pharmacokinetic properties

The absolute bioavailability of cetrorelix after subcutaneous administration is about 85%.

The total plasma clearance and the renal clearance are 1.2 ml x $min^{-1}$ x $kg^{-1}$ and 0.1 ml x $min^{-1}$ x $kg^{-1}$ , respectively. The volume of distribution ($V_d$) is 1.1 l x $kg^{-1}$. The mean terminal half-lives following intravenous and subcutaneous administration are about 12 h and 30 h, respectively, demonstrating the effect of absorption processes at the injection site. The subcutaneous administration of single doses (0.25 mg to 3 mg cetrorelix) and also daily dosing over 14 days show linear kinetics.

### 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

No target organ toxicity could be observed from acute, subacute and chronic toxicity studies in rats and dogs following subcutaneous administration of cetrorelix. No signs of medicinal product-related local irritation or incompatibility were noted in dogs after intravenous, intra-arterial and paravenous injection when cetrorelix was administered in doses clearly above the intended clinical use in man.

Cetrorelix showed no mutagenic or clastogenic potential in gene and chromosome mutation assays.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Powder:
Mannitol

Solvent:
Water for injections

### 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

### 6.3 Shelf life

2 years.

The solution should be used immediately after preparation.

### 6.4 Special precautions for storage

Do not store above 25 °C. Keep the vial(s) in the outer carton in order to protect from light.

### 6.5 Nature and contents of container

Packs with 1 or 7 Type I glass vials sealed with a rubber stopper.

Additionally for each vial the packs contain:

1 pre-filled syringe (Type I glass cartridge closed with rubber stoppers) with 1 ml solvent for parenteral use
1 injection needle (20 gauge)
1 hypodermic injection needle (27 gauge)
2 alcohol swabs.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

Cetrotide should only be reconstituted with the solvent provided, using a gentle, swirling motion. Vigorous shaking with bubble formation should be avoided.

The reconstituted solution is without particles and clear. Do not use if the solution contains particles or if the solution is not clear.

Withdraw the entire contents of the vial. This ensures a delivery to the patient of a dose of at least 0.23 mg cetrorelix.

The solution should be used immediately after reconstitution.

## 7. MARKETING AUTHORISATION HOLDER

Serono Europe Limited
56 Marsh Wall
London E14 9TP
United Kingdom

## 8. MARKETING AUTHORISATION NUMBER(S)

EU/1/99/100/001
EU/1/99/100/002

## 9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 April 1999
Date of first renewal: 15 April 2004
Date of latest renewal:

## 10. DATE OF REVISION OF THE TEXT

## 1. NAME OF THE MEDICINAL PRODUCT

Cetrotide 3 mg powder and solvent for solution for injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 3 mg cetrorelix (as acetate). After reconstitution with the solvent provided, each ml of the solution contains 3 mg cetrorelix.

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

Appearance of the powder: white lyophilisate
Appearance of the solvent: clear and colourless solution

The pH of the reconstituted solution is 4.0 – 6.0

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Prevention of premature ovulation in patients undergoing a controlled ovarian stimulation, followed by oocyte pick-up and assisted reproductive techniques.

In clinical trials Cetrotide was used with human menopausal gonadotropin (HMG), however, limited experience with recombinant follicule-stimulating hormone (FSH) suggested similar efficacy.

### 4.2 Posology and method of administration

Cetrotide should only be prescribed by a specialist experienced in this field.

The first administration of Cetrotide should be performed under the supervision of a physician and under conditions where treatment of possible allergic/pseudo-allergic reactions (including life-threatening anaphylaxis) is immediately available. The following injections may be self-administered as long as the patient is made aware of the signs and symptoms that may indicate hypersensitivity, the consequences of such a reaction and the need for immediate medical intervention.

The contents of 1 vial (3 mg cetrorelix) are to be administered on day 7 of ovarian stimulation (approximately 132 to 144 hours after start of ovarian stimulation) with urinary or recombinant gonadotropins. Following the first administration, it is advised that the patient be kept under medical supervision for 30 minutes to ensure there is no allergic/pseudo-allergic reaction to the injection.

If the follicle growth does not allow ovulation induction on the fifth day after injection of Cetrotide 3 mg, additionally 0.25 mg cetrorelix (Cetrotide 0.25 mg) should be administered once daily beginning 96 hours after the injection of Cetrotide 3 mg until the day of ovulation induction.

Cetrotide is for subcutaneous injection into the lower abdominal wall.

The injection site reactions may be minimised by injecting the product in a slow rate to facilitate the progressive absorption of the product.

Additional information on special populations:

There is no relevant indication for the use of Cetrotide in children or geriatric populations.

For instructions for preparation, see section 6.6.

## 4.3 Contraindications

- Hypersensitivity to the active substance or any structural analogues of gonadotropin-releasing hormone (GnRH), extrinsic peptide hormones or to any of the excipients.
- Pregnancy and lactation.
- Postmenopausal women.
- Patients with moderate and severe renal and hepatic impairment.

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Special care should be taken in women with signs and symptoms of active allergic conditions or known history of allergic predisposition. Treatment with Cetrotide is not advised in women with severe allergic conditions.

During or following ovarian stimulation an ovarian hyperstimulation syndrome can occur. This event must be considered as an intrinsic risk of the stimulation procedure with gonadotropins.

An ovarian hyperstimulation syndrome should be treated symptomatically, e.g. with rest, intravenous electrolytes/colloids and heparin therapy.

Luteal phase support should be given according to the reproductive medical centre´s practice.

There is limited experience up to now with the administration of Cetrotide during a repeated ovarian stimulation procedure. Therefore Cetrotide should be used in repeated cycles only after a careful risk/benefit evaluation.

## 4.5 Interaction with other medicinal products and other forms of interaction

*In vitro* investigations have shown that interactions are unlikely with medicinal products that are metabolised by cytochrome P450 or glucuronised or conjugated in some other way. However, although there has been no evidence of drug-interactions, especially with commonly used medicinal products, gonadotropins or products that may induce histamine release in susceptible individuals, the possibility of an interaction cannot be totally excluded.

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Studies in animals have indicated that cetrorelix exerts a dose related influence on fertility, reproductive performance and pregnancy. No teratogenic effects occurred when the medicinal product was administered during the sensitive phase of gestation.

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Cetrotide has no or negligible influence on the ability to drive or use machines.

## 4.8 Undesirable effects

The most commonly reported side effects are local injection site reactions such as erythema, swelling and pruritus that are usually transient in nature and mild in intensity.

Mild to moderate ovarian hyperstimulation syndrome (OHSS) (WHO grade I or II) have been commonly reported and should be considered as an intrinsic risk of the stimulation procedure. Inversely, severe OHSS remains uncommon.

Uncommonly, cases of hypersensitivity reactions including pseudo-allergic/anaphylactoid reactions have been reported.

The adverse reactions reported below are classified according to frequency of occurrence as follows:

| | |
|---|---|
| Very Common | ≥ 1/10 |
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Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

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|---|---|---|
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| Nervous system disorders | Uncommon | Headache |
| Gastrointestinal disorders | Uncommon | Nausea |
| Reproductive system and breast disorders | Common | Mild to moderate ovarian hyperstimulation syndrome (WHO grade I or II) can occur which is an intrinsic risk of the stimulation procedure (see section 4.4). |
| | Uncommon | Severe ovarian hyperstimulation syndrome (WHO grade III) |
| General disorders and administration site conditions | Common | Local reactions at the injection site (e.g. erythema, swelling and pruritus) have been reported. Usually they were transient in nature and of mild intensity. The frequency as reported in clinical trials was 8.0%. |

## 4.9 Overdose

Overdosage in humans may result in a prolonged duration of action but is unlikely to be associated with acute toxic effects.

In acute toxicity studies in rodents non-specific toxic symptoms were observed after intraperitoneal administration of cetrorelix doses more than 200 times higher than the pharmacologically effective dose after subcutaneous administration.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-gonadotropin-releasing hormones, ATC code: H01CC02.

Cetrorelix is a luteinising hormone releasing hormone (LHRH) antagonist. LHRH binds to membrane receptors on pituitary cells. Cetrorelix competes with the binding of endogenous LHRH to these receptors. Due to this mode of action, cetrorelix controls the secretion of gonadotropins (LH and FSH).

Cetrorelix dose-dependently inhibits the secretion of LH and FSH from the pituitary gland. The onset of suppression is virtually immediate and is maintained by continuous treatment, without initial stimulatory effect.

In females, cetrorelix delays the LH surge and consequently ovulation. In women undergoing ovarian stimulation the duration of action of cetrorelix is dose dependent. Following a single dose of 3 mg of cetrorelix a duration of action of at least 4 days has been evaluated. On day 4 the suppression was approximately 70%. At a dose of 0.25 mg per injection repeated injections every 24 hours will maintain the effect of cetrorelix.

In animals as well as in humans, the antagonistic hormonal effects of cetrorelix were fully reversible after termination of treatment.

### 5.2 Pharmacokinetic properties

The absolute bioavailability of cetrorelix after subcutaneous administration is about 85%.

The total plasma clearance and the renal clearance are 1.2 ml x $min^{-1}$ x $kg^{-1}$ and 0.1 ml x $min^{-1}$ x $kg^{-1}$ , respectively. The volume of distribution ($V_d$) is 1.1 l x $kg^{-1}$. The mean terminal half-lives following intravenous and subcutaneous administration are about 12 h and 30 h, respectively, demonstrating the effect of absorption processes at the injection site. The subcutaneous administration of single doses (0.25 mg to 3 mg cetrorelix) and also daily dosing over 14 days show linear kinetics.

### 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

No target organ toxicity could be observed from acute, subacute and chronic toxicity studies in rats and dogs following subcutaneous administration of cetrorelix. No signs of medicinal product-related local irritation or incompatibility were noted in dogs after intravenous, intra-arterial and paravenous injection when cetrorelix was administered in doses clearly above the intended clinical use in man.

Cetrorelix showed no mutagenic or clastogenic potential in gene and chromosome mutation assays.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Powder:
Mannitol

Solvent:
Water for injections

## 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

## 6.3 Shelf life

2 years.

The solution should be used immediately after preparation.

## 6.4 Special precautions for storage

Do not store above 25 °C. Keep the vial in the outer carton in order to protect from light.

## 6.5 Nature and contents of container

Pack with 1 Type I glass vial sealed with a rubber stopper.

Additionally the pack contains:

1 pre-filled syringe (Type I glass cartridge closed with rubber stoppers) with 3 ml solvent for parenteral use
1 injection needle (20 gauge)
1 hypodermic injection needle (27 gauge)
2 alcohol swabs.

## 6.6 Special precautions for disposal and other handling

Cetrotide should only be reconstituted with the solvent provided, using a gentle, swirling motion. Vigorous shaking with bubble formation should be avoided.

The reconstituted solution is without particles and clear. Do not use if the solution contains particles or if the solution is not clear.

Withdraw the entire contents of the vial. This ensures a delivery to the patient of a dose of at least 2.82 mg cetrorelix.

The solution should be used immediately after reconstitution.

# 7. MARKETING AUTHORISATION HOLDER

Serono Europe Limited
56 Marsh Wall
London E14 9TP
United Kingdom

# 8. MARKETING AUTHORISATION NUMBER(S)

EU/1/99/100/003

## 9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 April 1999
Date of first renewal: 15 April 2004
Date of latest renewal:

## 10. DATE OF REVISION OF THE TEXT

# ANNEX II

## A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

## B. CONDITIONS OF THE MARKETING AUTHORISATION

## A MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Baxter Oncology GmbH
Kantstraße 2
D-33790 Halle
Germany

Æterna Zentaris GmbH
Weismüllerstraße 50
D-60314 Frankfurt
Germany

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

## B CONDITIONS OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription.

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable

- **OTHER CONDITIONS**

*Risk Management Plan*

The MAH commits to performing pharmacovigilance activities detailed in version 2.0 (20/11/2008) of the Risk Management Plan (RMP) presented in Module 1.8.2 of the Marketing Authorisation and any subsequent updates of the RMP agreed by the CHMP.

As per the CHMP Guideline on Risk Management Systems for medicinal products for human use, any updated RMP should be submitted at the same time as the following Periodic Safety Update Report (PSUR).

In addition, an updated RMP should be submitted

When new information is received that may impact on the current Safety Specification, Pharmacovigilance Plan or risk minimisation activities

Within 60 days of an important (pharmacovigilance or risk minimisation) milestone being reached

At the request of the EMEA

*PSURs*

PSURs will have to be submitted with a 2-year frequency, until otherwise specified by the CHMP.

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**BOX OF 1 VIAL AND 1 PRE-FILLED SYRINGE**

## 1. NAME OF THE MEDICINAL PRODUCT

Cetrotide 0.25 mg powder and solvent for solution for injection
cetrorelix

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 vial with powder contains:
0.25 mg cetrorelix (as acetate).

## 3. LIST OF EXCIPIENTS

Excipient: Mannitol.
1 pre-filled syringe with solvent contains: 1 ml water for injections.

## 4. PHARMACEUTICAL FORM AND CONTENTS

1 vial with powder for solution for injection.
1 pre-filled syringe with solvent for parenteral use.
Additionally, the pack contains:
1 injection needle (20 gauge)
1 hypodermic injection needle (27 gauge)
2 alcohol swabs.

## 5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

## 8. EXPIRY DATE

EXP

## 9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C. Keep the vial in the outer carton in order to protect from light.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Serono Europe Limited
56 Marsh Wall
London E14 9TP
United Kingdom

## 12. MARKETING AUTHORISATION NUMBER(S)

EU/1/99/100/001

## 13. BATCH NUMBER

Batch

## 14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

## 15. INSTRUCTIONS ON USE

## 16. INFORMATION IN BRAILLE

cetrotide 0.25 mg

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**BOX OF 7 VIALS AND 7 PRE-FILLED SYRINGES**

## 1. NAME OF THE MEDICINAL PRODUCT

Cetrotide 0.25 mg powder and solvent for solution for injection
cetrorelix

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 vial with powder contains:
0.25 mg cetrorelix (as acetate).

## 3. LIST OF EXCIPIENTS

Excipient: Mannitol.
1 pre-filled syringe with solvent contains: 1 ml water for injections.

## 4. PHARMACEUTICAL FORM AND CONTENTS

7 vials with powder for solution for injection.
7 pre-filled syringes with solvent for parenteral use.
Additionally, the pack contains :
7 injection needle (20 gauge)
7 hypodermic injection needle (27 gauge)
14 alcohol swabs.

## 5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

## 8. EXPIRY DATE

EXP

## 9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C. Keep the vial(s) in the outer carton in order to protect from light.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Serono Europe Limited
56 Marsh Wall
London E14 9TP
United Kingdom

## 12. MARKETING AUTHORISATION NUMBER(S)

EU/1/99/100/002

## 13. BATCH NUMBER

Batch

## 14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

## 15. INSTRUCTIONS ON USE

## 16. INFORMATION IN BRAILLE

cetrotide 0.25 mg

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**CETROTIDE 0.25 MG VIAL LABEL**

## 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cetrotide 0.25 mg powder for solution for injection
cetrorelix
Subcutaneous use

## 2. METHOD OF ADMINISTRATION

Read the package leaflet before use

## 3. EXPIRY DATE

EXP

## 4. BATCH NUMBER

Batch

## 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.25 mg

## 6. OTHER

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**SOLVENT PRE-FILLED SYRINGE LABEL**

## 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for Cetrotide 0.25 mg
Water for injections

## 2. METHOD OF ADMINISTRATION

## 3. EXPIRY DATE

EXP

## 4. BATCH NUMBER

Batch

## 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

## 6. OTHER

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**BOX OF 1 VIAL AND 1 PRE-FILLED SYRINGE**

## 1. NAME OF THE MEDICINAL PRODUCT

Cetrotide 3 mg powder and solvent for solution for injection
cetrorelix

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 vial with powder contains:
3 mg cetrorelix (as acetate).

## 3. LIST OF EXCIPIENTS

Excipient: Mannitol.
1 pre-filled syringe with solvent contains: 3 ml water for injections.

## 4. PHARMACEUTICAL FORM AND CONTENTS

1 vial with powder for solution for injection.
1 pre-filled syringe with solvent for parenteral use.
Additionally, the pack contains:
1 injection needle (20 gauge)
1 hypodermic injection needle (27 gauge)
2 alcohol swabs.

## 5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

## 8. EXPIRY DATE

EXP

## 9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C. Keep the vial in the outer carton in order to protect from light.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Serono Europe Limited
56 Marsh Wall
London E14 9TP
United Kingdom

## 12. MARKETING AUTHORISATION NUMBER(S)

EU/1/99/100/003

## 13. BATCH NUMBER

Batch

## 14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

## 15. INSTRUCTIONS ON USE

## 16. INFORMATION IN BRAILLE

cetrotide 3 mg

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**CETROTIDE 3 MG VIAL LABEL**

## 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cetrotide 3 mg powder for solution for injection
cetrorelix
Subcutaneous use

## 2. METHOD OF ADMINISTRATION

Read the package leaflet before use

## 3. EXPIRY DATE

EXP

## 4. BATCH NUMBER

Batch

## 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mg

## 6. OTHER

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**SOLVENT PRE-FILLED SYRINGE LABEL**

## 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for Cetrotide 3 mg
Water for injections

## 2. METHOD OF ADMINISTRATION

## 3. EXPIRY DATE

EXP

## 4. BATCH NUMBER

Batch

## 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml

## 6. OTHER

**B. PACKAGE LEAFLET**

**PACKAGE LEAFLET: INFORMATION FOR THE USER**

**Cetrotide 0.25 mg powder and solvent for solution for injection**

**Cetrorelix**

**Read all of this leaflet carefully before you start using this medicine.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

**In this leaflet**:


## 1. WHAT CETROTIDE IS AND WHAT IT IS USED FOR

Cetrotide blocks the receptors of a natural hormone, called luteinising hormone releasing hormone (LHRH) and thus indirectly the effect of this hormone. LHRH controls the production and release of another hormone, called luteinising hormone (LH) which stimulates ovulation during the menstrual cycle.

Cetrotide is used to prevent the premature release of LH and thus, the premature release from the ovaries of an egg (oocyte) (i.e. premature ovulation) that may be immature. Premature ovulation is actually undesirable during treatment inducing ovaries to produce more eggs (ovarian stimulation) as premature release of LH triggers oocytes release before it is possible to collect them (oocyte pick-up) by a simple procedure for assisted reproductive technologies.

In clinical trials Cetrotide was used with human menopausal gonadotropin (HMG). Limited, post-marketing experience with another hormone, i.e. recombinant follicle stimulating hormone (FSH) suggested similar efficacy. HMG and FSH are hormones promoting egg maturation.

## 2. BEFORE YOU USE CETROTIDE

**Do not use Cetrotide**

- if you are allergic (hypersensitive) to cetrorelix acetate, exogenous peptide hormones (medicines similar to Cetrotide) or any of the other ingredients.
- if you are pregnant or breast-feeding
- if you have already reached your menopause
- if you have a moderate or severe kidney or liver disease.

**Take special care with Cetrotide**

Special care should be taken in women with an active allergic condition or a known history of allergy. If you present such a condition, it is important that you inform your doctor.

During or following hormonal stimulation of the ovaries an ovarian hyperstimulation syndrome can occur. This event is related to the stimulation procedure with gonadotropins (hormones promoting egg maturation). For symptoms and suitable measures please refer to the Patient Information Leaflet of the gonadotropin-containing medicine prescribed for you.

Luteal phase support (a measure to increase the uterus receptivity to embryo implantation and to support early pregnancy, generally by administering progesterone or human chorionic gonadotropin) should be given according to the reproductive medical centre's practice.

Because experience of using Cetrotide during repeated ovarian stimulation procedures is still small, you should use the medicine in repeated cycles only after your doctor has carefully evaluated the benefits and risks.

**Using other medicines**

*In vitro* investigations have shown that interactions are unlikely with medicines that are degraded by the liver. However, though there has been no evidence of drug- interactions, especially with commonly used medicines, gonadotropins or products that may induce histamine release in susceptible individuals, the possibility of an interaction cannot be totally excluded.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

**Pregnancy and breast-feeding**

You must not use Cetrotide if you are already pregnant, or suspect that you might be pregnant, or if you are breast-feeding.

**Driving and using machines**

The use of Cetrotide is not expected to affect your ability to drive and use machines.

## 3. HOW TO USE CETROTIDE

Always use Cetrotide exactly as your doctor has told you. You should check with your doctor if you are not sure. The following statements apply to Cetrotide unless otherwise prescribed by your doctor. Please observe these instructions for use, otherwise you will not fully benefit from Cetrotide.

Cetrotide is intended for subcutaneous use, that means given by injection just under the skin. It is for single use only.

The first injection of Cetrotide should be supervised by your doctor. You can carry out the following injections yourself as long as your doctor has made you aware of the symptoms that may indicate allergy and of its consequences (serious, potentially life-threatening allergic reaction, causing difficulty in breathing or dizziness, may occur and need immediate treatment).

Cetrotide is for injection under the skin of the lower abdominal wall, preferably around the navel. To minimise local irritation, please select a different injection site each day and inject slowly.

Dissolve Cetrotide powder only with the water contained in the pre-filled syringe. Do not use a Cetrotide solution if it is not clear or contains particles.

**Before you administer Cetrotide yourself, please read the following instructions carefully**

1. Wash your hands. Your hands and all items you use should be as clean as possible.

2. Lay out on a clean surface everything you need (one vial, one pre-filled syringe, one injection needle with a yellow mark, one injection needle with a grey mark and two alcohol swabs).

3. Flip off the plastic cover of the vial. Wipe the aluminium ring and the rubber stopper with an alcohol swab.

4. Take the injection needle with the yellow mark and remove the wrapping. Take the pre-filled syringe and remove the cover. Put the needle on the syringe and remove the cover of the needle.

5. Push the needle through the centre of the rubber stopper of the vial. Inject the water into the vial by slowly pushing the plunger of the syringe.

6. Leave the syringe on the vial. Gently agitate the vial until the solution is clear and without residue. Avoid forming bubbles during dissolution.

7. Draw the whole contents of the vial into the syringe. If solution is left in the vial, invert the vial, pull back the needle until the opening of the needle is just inside the stopper. If you look from the side through the gap in the stopper, you can control the movement of the needle and the liquid. Make sure that you withdraw the entire contents of the vial.

8. Detach the syringe from the needle and lay down the syringe. Take the injection needle with the grey mark and remove its wrapping. Put the needle on the syringe and remove the cover of the needle.

9. Invert the syringe and push the plunger until all air bubbles have been expelled. Do not touch the needle or allow the needle to touch any surface.

10. Choose an injection site at the lower abdominal wall, preferably around the navel. Take the second alcohol swab and clean the skin at the injection site. Hold the syringe in one hand. Gently pinch up the skin surrounding the site of injection and hold firmly with the other hand.

11. Hold the syringe as you would hold a pencil, insert the needle completely into the skin at an angle of about 45 degree.

12. Once the needle has been inserted completely, release your grasp of the skin.

13. Pull back gently the plunger of the syringe. If blood appears continue as described in step 14. If no blood appears, inject the solution slowly by pushing the plunger gently forward. After all of the solution is injected, withdraw the needle slowly, applying gentle pressure with the alcohol swab on the skin where the needle was inserted. Withdraw the needle at the same angle as it was inserted.

14. If blood appears, withdraw the needle with the syringe and gently apply pressure to the injection site. Do not use this solution but empty the syringe in a sink. Start again with step 1.

15. Use the syringe and needles only once. Throw away the syringe and needles immediately after use (put the covers on the needles to avoid injury).

The contents of one vial (0.25 mg cetrorelix) are to be injected once daily, at 24 h intervals, either in the morning or in the evening.

Administration in the morning: Treatment with Cetrotide should begin on day 5 or 6 of ovarian stimulation (approximately 96 to 120 hours after start of ovarian stimulation) with urinary or recombinant gonadotropin(s) and is to be continued throughout the ovarian stimulation treatment period including the day of ovulation induction.

Administration in the evening: Treatment with Cetrotide should begin on day 5 of ovarian stimulation (approximately 96 to 108 hours after start of ovarian stimulation) with urinary or recombinant gonadotropin(s) and is to be continued throughout the ovarian stimulation treatment period until the evening prior to the day of ovulation induction.

**If you use more Cetrotide than you should**

Overdosage of Cetrotide may result in a prolonged duration of action but is unlikely to be associated with sudden untoward/damaging effects. Therefore, in case of overdosage no specific measures are required.

**If you forget to take Cetrotide**

Do not take a double dose to make up for a forgotten dose, please contact your doctor.

Ideally Cetrotide should be injected at 24 hours intervals. But if you missed giving it at the right time you can inject this dose at a different time of the same day.

## 4. POSSIBLE SIDE EFFECTS

Like all medicines, Cetrotide can cause side effects, although not everybody gets them.

If you experience severe generalised allergic reactions such as difficulty in breathing or dizziness which could be potentially life-threatening, stop using Cetrotide, contact your doctor immediately or seek urgent medical attention.

The frequency of possible side effects listed below is defined using the following convention:
very common: affects more than 1 user in 10
common: affects 1 to 10 users in 100
uncommon: affects 1 to 10 users in 1,000
rare: affects 1 to 10 users in 10,000
very rare: affects less than 1 user in 10,000

Common:
- Mild and transient reactions may occur at the injection site like reddening, itching, and swelling.
- Mild to moderate ovarian hyperstimulation syndrome (OHSS). Symptoms like abdominal pain, tension, nausea, vomiting and diarrhoea may indicate an OHSS. If you feel such symptoms, please inform your doctor immediately.

Uncommon:
- Severe generalised allergic reactions (including serious, potentially life-threatening allergic reaction which causes difficulty in breathing or dizziness).
- Severe ovarian hyperstimulation syndrome (OHSS). Symptoms may be abdominal pain, abdominal distension, nausea, vomiting, diarrhoea, weight gain, reduced urine flow and breathing difficulties. Complications may include blood clotting. If you feel such symptoms, please inform your doctor immediately.
- Nausea.
- Headache.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

## 5. HOW TO STORE CETROTIDE

Keep out of the reach and sight of children.

Do not use Cetrotide after the expiry date which is stated on the vial after EXP. The expiry date refers to the last day of that month.
The Cetrotide powder in the vial and the solvent in the pre-filled syringe have the same expiry date. It is printed on the labels and on the carton.

Do not store above 25°C.

Keep the vial in the outer carton in order to protect from light.

The solution should be used immediately after preparation.

Do not use Cetrotide if the white pellet in the vial has changed in appearance or if the solvent solution in the vial is no longer clear and colourless or if it contains particles.

If you have any further questions please consult your doctor or pharmacist.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

## 6. FURTHER INFORMATION

**What Cetrotide contains**

Each vial contains 0.25 mg cetrorelix (as acetate).

The other ingredient is mannitol.

The solvent is Water for injections.

**What Cetrotide looks like and contents of the pack**

Cetrotide is a white powder for solution for injection. It is available in packs of one or seven vials.

Additionally, for each vial the packs contain
- one pre-filled syringe with solvent (water for injections) for parenteral use for dissolving the powder in the vial
- one injection needle with a yellow mark for injecting the water into the vial and withdrawing the solution from the vial
- one injection needle with a grey mark for injecting the solution
- two alcohol swabs for cleaning purposes.

**Marketing Authorisation Holder**

Serono Europe Limited, 56 Marsh Wall, London E14 9TP,United Kingdom

**Manufacturer**

Baxter Oncology GmBH, Kantstrasse 2, D-33790 Halle, Germany
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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**PACKAGE LEAFLET: INFORMATION FOR THE USER**

**Cetrotide 3 mg powder and solvent for solution for injection**

**Cetrorelix**

**Read all of this leaflet carefully before you start using this medicine.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
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**In this leaflet**:


## 1. WHAT CETROTIDE IS AND WHAT IT IS USED FOR

Cetrotide blocks the receptors of a natural hormone, called luteinising hormone releasing hormone (LHRH) and thus indirectly the effect of this hormone. LHRH controls the production and release of another hormone, called luteinising hormone (LH) which stimulates ovulation during the menstrual cycle.

Cetrotide is used to prevent the premature release of LH and thus, the premature release from the ovaries of an egg (oocyte) (i.e. premature ovulation) that may be immature. Premature ovulation is actually undesirable during treatment inducing ovaries to produce more eggs (ovarian stimulation) as premature release of LH triggers oocytes release before it is possible to collect them (oocyte pick-up) by a simple procedure for assisted reproductive technologies.

In clinical trials Cetrotide was used with human menopausal gonadotropin (HMG). Limited, post-marketing experience with another hormone, i.e. recombinant follicle stimulating hormone (FSH) suggested similar efficacy. HMG and FSH are hormones promoting egg maturation.

## 2. BEFORE YOU USE CETROTIDE

**Do not use Cetrotide**

- if you are allergic (hypersensitive) to cetrorelix acetate, exogenous peptide hormones (medicines similar to Cetrotide) or any of the other ingredients.
- if you are pregnant or breast-feeding
- if you have already reached your menopause
- if you have a moderate or severe kidney or liver disease.

**Take special care with Cetrotide**

Special care should be taken in women with an active allergic condition or a known history of allergy. If you present such a condition, it is important that you inform your doctor.

During or following hormonal stimulation of the ovaries an ovarian hyperstimulation syndrome can occur. This event is related to the stimulation procedure with gonadotropins (hormones promoting egg maturation). For symptoms and suitable measures please refer to the Patient Information Leaflet of the gonadotropin-containing medicine prescribed for you.

Luteal phase support (a measure to increase the uterus receptivity to embryo implantation and to support early pregnancy, generally by administering progesterone or human chorionic gonadotropin) should be given according to the reproductive medical centre's practice.

Because experience of using Cetrotide during repeated ovarian stimulation procedures is still small, you should use the medicine in repeated cycles only after your doctor has carefully evaluated the benefits and risks.

**Using other medicines**

*In vitro* investigations have shown that interactions are unlikely with medicines that are degraded by the liver. However, though there has been no evidence of drug- interactions, especially with commonly used medicines, gonadotropins or products that may induce histamine release in susceptible individuals, the possibility of an interaction cannot be totally excluded.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

**Pregnancy and breast-feeding**

You must not use Cetrotide if you are already pregnant, or suspect that you might be pregnant, or if you are breast-feeding.

**Driving and using machines**

The use of Cetrotide is not expected to affect your ability to drive and use machines.

## 3. HOW TO USE CETROTIDE

Always use Cetrotide exactly as your doctor has told you. You should check with your doctor if you are not sure. The following statements apply to Cetrotide unless otherwise prescribed by your doctor. Please observe these instructions for use, otherwise you will not fully benefit from Cetrotide.

Cetrotide is intended for subcutaneous use, that means given by injection just under the skin. It is for single use only.

The first injection of Cetrotide should be supervised by your doctor. You can carry out the following injections yourself as long as your doctor has made you aware of the symptoms that may indicate allergy and of its consequences (serious, potentially life-threatening allergic reaction, causing difficulty in breathing or dizziness, may occur and need immediate treatment).

Cetrotide is for injection under the skin of the lower abdominal wall, preferably around the navel. To minimise local irritation, please inject slowly.

Dissolve Cetrotide powder only with the water contained in the pre-filled syringe. Do not use a Cetrotide solution if it is not clear or contains particles.

**Before you administer Cetrotide yourself, please read the following instructions carefully**

1. Wash your hands. Your hands and all items you use should be as clean as possible.

2. Lay out on a clean surface everything you need (one vial, one pre-filled syringe, one injection needle with a yellow mark, one injection needle with a grey mark and two alcohol swabs).

3. Flip off the plastic cover of the vial. Wipe the aluminium ring and the rubber stopper with an alcohol swab.

4. Take the injection needle with the yellow mark and remove the wrapping. Take the pre-filled syringe and remove the cover. Put the needle on the syringe and remove the cover of the needle.

5. Push the needle through the centre of the rubber stopper of the vial. Inject the water into the vial by slowly pushing the plunger of the syringe.

6. Leave the syringe on the vial. Gently agitate the vial until the solution is clear and without residue. Avoid forming bubbles during dissolution.

7. Draw the whole contents of the vial into the syringe. If solution is left in the vial, invert the vial, pull back the needle until the opening of the needle is just inside the stopper. If you look from the side through the gap in the stopper, you can control the movement of the needle and the liquid. Make sure that you withdraw the entire contents of the vial.

8. Detach the syringe from the needle and lay down the syringe. Take the injection needle with the grey mark and remove its wrapping. Put the needle on the syringe and remove the cover of the needle.

9. Invert the syringe and push the plunger until all air bubbles have been expelled. Do not touch the needle or allow the needle to touch any surface.

10. Choose an injection site at the lower abdominal wall, preferably around the navel. Take the second alcohol swab and clean the skin at the injection site. Hold the syringe in one hand. Gently pinch up the skin surrounding the site of injection and hold firmly with the other hand.

11. Hold the syringe as you would hold a pencil, insert the needle completely into the skin at an angle of about 45 degree.

12. Once the needle has been inserted completely, release your grasp of the skin.

13. Pull back gently the plunger of the syringe. If blood appears continue as described in step 14. If no blood appears, inject the solution slowly by pushing the plunger gently forward. After all of the solution is injected, withdraw the needle slowly, applying gentle pressure with the alcohol swab on the skin where the needle was inserted. Withdraw the needle at the same angle as it was inserted.

14. If blood appears, withdraw the needle with the syringe and gently apply pressure to the injection site. Do not use this solution but empty the syringe in a sink.

15. Use the syringe and needles only once. Throw away the syringe and needles immediately after use (put the covers on the needles to avoid injury).

The contents of 1 vial (3 mg cetrorelix) are to be injected on day 7 of ovarian stimulation (approximately 132 to 144 hours after start of ovarian stimulation) with urinary or recombinant gonadotropins.

A single dose of Cetrotide 3 mg results in a duration of action of at least 4 days. If the follicle growth does not allow ovulation induction on the fifth day after injection of Cetrotide 3 mg, additionally 0.25 mg cetrorelix (Cetrotide 0.25 mg) should be administered once daily beginning 96 hours after the injection of Cetrotide 3 mg until the day of ovulation induction.

**If you use more Cetrotide than you should**

Overdosage of Cetrotide may result in a prolonged duration of action but is unlikely to be associated with sudden untoward/damaging effects. Therefore, in case of overdosage no specific measures are required.

**If you forget to take Cetrotide**

Do not take a double dose to make up for a forgotten dose, please contact your doctor.

## 4. POSSIBLE SIDE EFFECTS

Like all medicines, Cetrotide can cause side effects, although not everybody gets them.

If you experience severe generalised allergic reactions such as difficulty in breathing or dizziness which could be potentially life-threatening, stop using Cetrotide, contact your doctor immediately or seek urgent medical attention.

The frequency of possible side effects listed below is defined using the following convention:
very common: affects more than 1 user in 10
common: affects 1 to 10 users in 100
uncommon: affects 1 to 10 users in 1,000
rare: affects 1 to 10 users in 10,000
very rare: affects less than 1 user in 10,000

Common:
- Mild and transient reactions may occur at the injection site like reddening, itching, and swelling.
- Mild to moderate ovarian hyperstimulation syndrome (OHSS). Symptoms like abdominal pain, tension, nausea, vomiting and diarrhoea may indicate an OHSS. If you feel such symptoms, please inform your doctor immediately.

Uncommon:
- Severe generalised allergic reactions (including serious, potentially life-threatening allergic reaction which causes difficulty in breathing or dizziness).
- Severe ovarian hyperstimulation syndrome (OHSS). Symptoms may be abdominal pain, abdominal distension, nausea, vomiting, diarrhoea, weight gain, reduced urine flow and breathing difficulties. Complications may include blood clotting. If you feel such symptoms, please inform your doctor immediately.
- Nausea.
- Headache.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

## 5. HOW TO STORE CETROTIDE

Keep out of the reach and sight of children.

Do not use Cetrotide after the expiry date which is stated on the vial after EXP. The expiry date refers to the last day of that month.
The Cetrotide powder in the vial and the solvent in the pre-filled syringe have the same expiry date. It is printed on the labels and on the carton.

Do not store above 25°C.

Keep the vial in the outer carton in order to protect from light.

The solution should be used immediately after preparation.

Do not use Cetrotide if the white pellet in the vial has changed in appearance or if the solvent solution in the vial is no longer clear and colourless or if it contains particles.

If you have any further questions please consult your doctor or pharmacist.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

## 6. FURTHER INFORMATION

**What Cetrotide contains**

Each vial contains 3 mg cetrorelix (as acetate)

The other ingredient is mannitol.

The solvent is Water for injections.

**What Cetrotide looks like and contents of the pack**

Cetrotide is a white powder for solution for injection. It is available in a pack with one vial.

Additionally, the pack contains
- one pre-filled syringe with solvent (water for injections) for parenteral use for dissolving the powder in the vial
- one injection needle with a yellow mark for injecting the water into the vial and withdrawing the solution from the vial
- one injection needle with a grey mark for injecting the solution
- two alcohol swabs for cleaning purposes.

**Marketing Authorisation Holder**

Serono Europe Limited, 56 Marsh Wall, London E14 9TP,United Kingdom

**Manufacturer**

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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